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The effects of 5-azacytidine and 5-azadeoxycytidine on chromosome structure and function: implications for methylation-associated cellular processes.

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5-Azacytidine (5-aza-C) analogs demonstrate a remarkable ability to induce heritable changes in gene and phenotypic expression. These cellular processes are associated with the demethylation of specific DNA sequences. On the other hand, 5-aza-C analogs have dramatic effects on chromosomes, leading to decondensation of chromatin structure, chromosomal instability and an advance in replication timing. Condensation inhibition of genetically inactive chromatin occurs when the DNA is still hemimethylated or fully methylated. In cell cultures prolonged for several replication cycles, chromosomal rearrangements and instability affect the 5-aza-C-sensitive regions. Moreover, the normally late-replicating inactive chromatin undergoes a transient temporal shift to an earlier DNA replication, characteristic of activatable chromatin. zThe induced alterations of chromosome structure and behavior may trigger the 5-aza-C-dependent process of cellular reprogramming. Apart from their differentiating and gene-modifying effects, 5-aza-C analogs can tumorigenically transform cells and modulate their metastatic potential. High doses of 5-aza-C analogs have cytotoxic and antineoplastic activities. (225 Refs.)

Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: *Antineoplastic Agents--Pharmacology--PD; *Azacitidine --Analogs and Derivatives--AA; *Azacitidine--Pharmacology--PD; *Chromosomes--Drug Effects--DE; *Chromosomes--Ultrastructure--UL; Carcinogens--Toxicity--TO; DNA Replication--Drug Effects--DE; Methylation
CAS Registry No.: 0 (Antineoplastic Agents); 0 (Carcinogens); 2353-33-5 (5-aza-2'-deoxycytidine); 320-67-2 (Azacitidine)